

NewsScan

NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

Research News

Hostility Personality Trait Predicts Brain Metabolic Response to Nicotine

People prone to anger and aggression may be predisposed to develop an addiction to nicotine compared with those who have happy, relaxed personalities, report NIDA-supported researchers.

Dr. Steven Potkin and colleagues at the University of California, Irvine, administered personality tests to 31 smokers and 55 nonsmokers. Participants were grouped according to hostile (anger, impatience, irritability, nervousness) or nonhostile (happy, relaxed, and curious) personality traits. All hostile and nonhostile smokers and nonsmokers received a low-dose nicotine patch, as well as a placebo. The hostile and nonhostile smokers also received a high-dose nicotine patch that produced blood levels of the chemical comparable to smoking a cigarette. The researchers used positron emission tomography (PET) to measure the participants' brain metabolic activity while performing an aggression task.

The PET scans showed no metabolic changes in the brains of low-hostility smokers and nonsmokers in response to either dose of nicotine. When the researchers analyzed PET scans from the high-hostility smokers and nonsmokers they found that the high-dose nicotine patch induced dramatic metabolic responses in the brains of smokers, while the low-dose nicotine patch elicited changes in the brains of nonsmokers. These changes occurred in the parts of the brain that control emotion, social response, attention, and language.

Thus, persons easy to anger have an increased brain response to nicotine, the scientists say. Since this occurs in smokers and nonsmokers it may help explain why people who are easy to anger are more susceptible to becoming addicted to cigarettes.

- **WHAT IT MEANS:** These findings may help explain why some people are more likely to become addicted to nicotine or express more of the mood consequences of trying to quit.

This study was published in the February 2004 issue of *Cognitive Brain Research*.

PET Scans Show Cocaine Addicts Have Generalized Decrease in D₂ Receptors Throughout Striatum

A new study builds on previous research showing that cocaine-addicted people have a low expression of specific dopamine receptors—D₂ receptors—in a portion of the brain called the striatum. The new findings demonstrate that cocaine-addicted people have decreased D₂ receptors in a generalized fashion throughout the various subdivisions of this brain region.

In addition, the researchers found that the decrease in the number of these receptors extended beyond parts of the striatum associated with pleasure or cognition to parts associated with movement. Although the significance of this finding is not known, it was unexpected, the scientists report.

In the study, 17 healthy control subjects and 17 recently detoxified drug-addicted subjects, who reported smoking crack cocaine 4 days per week for about 15 years, underwent positron emission tomography (PET) scanning that allowed the scientists to observe their brain biochemistry.

The D₂ receptor is one of five in the brain associated with the chemical dopamine, which is thought to regulate reward and some behaviors, such as sex and eating. Previous research

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suggests that drugs of abuse activate the brain's dopamine system. The discharge of dopamine in the brain creates a pleasurable sensation, prompting a craving for more of the substance that triggered its release. The D₂ receptor may help power that craving.

The brain scans confirmed that people who are dependent on cocaine have fewer D₂ receptors and that this decrease is evident throughout the striatum.

The scientists also hypothesized the decrease in D₂ receptors would be associated with maintaining the addictive behavior. However, they found no relationship between the number of these dopamine receptors and the subjects' perception of cocaine's pleasurable effects and their drug-seeking behavior.

- **WHAT IT MEANS:** People who are dependent on cocaine experience a decrease in D₂ receptors, but it remains unknown at present if this decrease predisposes someone to be vulnerable to cocaine addiction or if it is a consequence of cocaine exposure. This decrease in D₂ receptors also may be more widespread than previously thought, affecting brain regions involved with movement, as well as motivation. Future studies may be warranted to establish the significance of these findings.

Dr. Diana Martinez and her colleagues at Columbia University published this NIDA-funded study in the online March 2004 issue of *Neuropsychopharmacology*.

In Treating Co-Occurring Disorders, Target Both Depression and Substance Abuse

A meta-analysis of 14 studies involving patients with co-occurring depression and alcohol or drug abuse suggests that using antidepressant medication to treat people with these disorders is beneficial, but that clinicians also should use concurrent therapy specifically targeting the addiction.

Dr. Edward Nunes and Dr. Frances Levin analyzed 14 studies that examined whether symptoms of depression respond to antidepressant medication in substance-addicted people and the impact of such treatment on concurrent substance abuse. The studies included 848 patients with depression and drug addictions. Eight trials recruited alcoholic patients, four recruited methadone-maintained, opiate-addicted patients, and two recruited cocaine-addicted patients. All of the studies were randomized, double-blind, and placebo-controlled.

The researchers found that antidepressant medication exerts a beneficial effect on depression in patients with alcohol or drug addiction, especially when the medications are used at adequate doses, for at least 6 weeks, and for depressive syndromes identified by clinical history and established diagnostic criteria. Their analysis also showed that even when medication is effective in treating depression, it helps bring about only a modest decrease in substance abuse. For this reason, they recommend clinicians also use therapies that directly treat the addiction.

- **WHAT IT MEANS:** Clinicians working with patients who have co-occurring drug abuse and depression may be reluctant to initiate antidepressant treatment because of a belief the depression may be temporary, or concern that focus on depression will detract from the treatment of substance abuse. This analysis supports recent recommendations that drug or alcohol abuse are not barriers to treating depression. The researchers also suggest additional research is needed to refine diagnostic methods that would allow clinicians to better distinguish substance abuse patients who would benefit from antidepressant therapy.

The scientists, both with the New York State Psychiatric Institute and Columbia University, published their findings in the April 21, 2004 issue of the *Journal of the American Medical Association*. Their research was partly funded by NIDA.

Long-Lasting Craving for Cocaine

Imagine you are a rat trained to obtain food by pressing a lever. One day, as you press the lever, you hear a burst of noise and simultaneously receive a jolt of intravenous cocaine. What do you do when you hear the noise again?

Rats in the study of Dr. Roberto Ciccocioppo learned to press the lever more vigorously when the noise occurred even if they received no more cocaine. After a single exposure to cocaine, the rats continued to respond to the noise with vigorous lever pressing for nearly a year.

Dr. Ciccocioppo, of Italy's University of Camerino, and his colleagues, Dr. Friedbert Weiss and Dr. Remi Martin-Fardon, from The Scripps Research Institute, then used the same conditioning methodology with a different group of rats, but substituted sweetened condensed milk—a powerful, nondrug incentive—as the unexpected reward. These animals stopped responding to the noise in less than 3 months.

- **WHAT IT MEANS:** An association-driven conditioned response to seek cocaine can persist for long periods even after a single dose. Drug-related experiences leave a much more powerful and longer-lasting impression than stimuli linked to conventional rewards. Such responses may play important roles in drug relapse.

This NIDA-funded study was published online March 28, 2004 in *Nature Neuroscience*.

Study Finds Communities Will Provide Support for MI Programs

Motivational incentive (MI) treatment has been shown to be effective in treating a range of substance abuse disorders—from smoking to cocaine addiction. During MI, participants earn positive rewards when they abstain from abusing substances for a given amount of time. The rewards in many MI studies have been in the form of vouchers that can be exchanged for goods and services. However, the cost of supporting the rewards used in MI limits its use by community treatment providers. Drs. Leslie Amass and Jonathan B. Kamien at the Friends Research Institute, Inc., in Los Angeles, California, found that when asked, community members, merchants, and companies will donate goods and services to help support an MI program designed to help pregnant, postpartum, and parenting substance abusers stop smoking.

Before soliciting donations, the researchers surveyed their clients to identify goods and services that would be incentives for them to abstain from smoking. Based on the results, the researchers developed a telephone and direct mail campaign targeted to potential sources for community sponsorship that included goods and services for babies, children, and women; toys; general goods and services; household needs; self-improvement; and entertainment. Campaigns were conducted in Toronto and Los Angeles.

During 2 months of active fundraising in Toronto, about 19 percent of those contacted donated an average of US\$4,000 per month in goods and services. In Los Angeles, about 26 percent of those contacted over 34 months gave an average of \$4,472 per month. More than 25 percent of the Los Angeles donors contributed to the program more than once. The researchers also found that after the fundraising campaign was established, one person devoting about one day per week could maintain the entire operation.

- **WHAT IT MEANS:** Donations can be garnered from businesses and individuals in local communities at a consistent rate and in amounts sufficient to sustain a typical MI program for pregnant, postpartum, and parenting substance abusers.

The findings were published in the May 2004 issue of *Experimental and Clinical Psychopharmacology*. The Los Angeles arm of the study was funded in part by NIDA.

Complex Genetics Tied to High Cost of Brain Disorders; Majority of Costs Related to Addiction

Researchers from NIDA and The Johns Hopkins University School of Medicine report that more than 40 percent of the costs associated with brain and nervous system disorders are related to genetics, and the largest single portion of these costs are due to addictions.

The scientists point out that the costs are not solely related to healthcare, but also include dollars spent on nontreatment practices, such as incarceration.

Brain and nervous system disorders may cost the United States more than \$1 trillion annually, and much of this burden stems from the influence of complex genetic factors rather than single-gene effects. At least 40 percent of addiction vulnerability among the U.S. population is genetic, and almost all of that is due to the effects of multiple genes. The researchers estimate that the American public spends more than \$200 billion on annual costs related to addiction.

- **WHAT IT MEANS:** Increasing what we know about genetic susceptibility to brain and nervous system diseases, including addictions, can enhance our ability to prevent the development of such disorders and reduce the economic costs associated with them. Researchers should be encouraged to investigate gene variants, as well as environmental factors, that influence the development of these diseases.

Dr. George Uhl and Dr. Robert Grow published their study in the March 2004 issue of the *Archives of General Psychiatry*.

NIDA Grantees Receive AACE Award

Dr. Leslie Miller and her colleagues at Rice University in Houston, Texas, were among those who received Outstanding Paper Awards for presentations at the World Conference on Educational Multimedia, Hypermedia and Telecommunications. The meeting was a function of the Association for the Advancement of Computing in Education (AACE).

Dr. Miller's activities are funded by a Science Education Drug Abuse Partnership Award from NIDA. The posters—"Using Web-based Multimedia Narrative and Simulations to Teach about Drugs of Abuse" and "Two Types of Web Adventure Games: Feedback from Users"—may be viewed on the AACE Digital Library at <http://rd.aace.org/awards/edmedia/2004/>.

Dr. Miller's current research at Rice's Center for Technology in Teaching and Learning focuses on the use of technology in education, in particular, envisioning new ways to use multimedia to improve learning among adolescents. Two Web-based projects, funded by NIDA, feature *The Reconstructors*®, an adventure set in the year 2254 and illustrated in a comic book style. The series, *A PLAGUING PROBLEM*, engages students in "reconstructing" the history and neurobiology of opioids. A second series, *NOTHING TO RAVE ABOUT*, deals with club drugs. These are freely available at <http://reconstructors.rice.edu>.

For more information about any item in this *NewsScan*:

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The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports more than 85 percent of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics are available in English and Spanish. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at <http://www.drugabuse.gov>.

(33)



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